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Gene Section
Review

ABCC10 (ATP-binding cassette, sub-family C (CFTR/MRP), member 10)

Elizabeth Hopper-Borge, Natalya Domanitskaya

Fox Chase Cancer Center, Developmental Therapeutics Program, Philadelphia, PA, USA (EHB, ND)

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Abstract

Review on ABCC10, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: EST182763, MRP7, SIMRP7

HGNC (Hugo): ABCC10

Location: 6p21.1

DNA/RNA

Note

Contains 22 exons and 21 introns (Kao et al., 2003).

Description

The gene encompasses 23065 bases.

Transcription

Transcript is 744 bps, and has 10 splice variants.

In normal tissue

A study of the ABCC10 promoter revealed that the presence of E2F and Sp1 sites are required for maximum transcription.

In addition other elements were found in the promoter including: cAMP-responsive element binding protein, estrogen receptor binding site, hepatic nuclear factor, progesterone receptor binding site, and sterol regulatory element binding protein (Dabrowska and Sirotnak, 2004).

ABCC10 transcript is widespread at low levels (Hopper et al., 2001; Maher et al., 2005) with highest expression in the pancreas. Decreased expression is observed in activated resting T and B cells (Takayanagi et al., 2004).

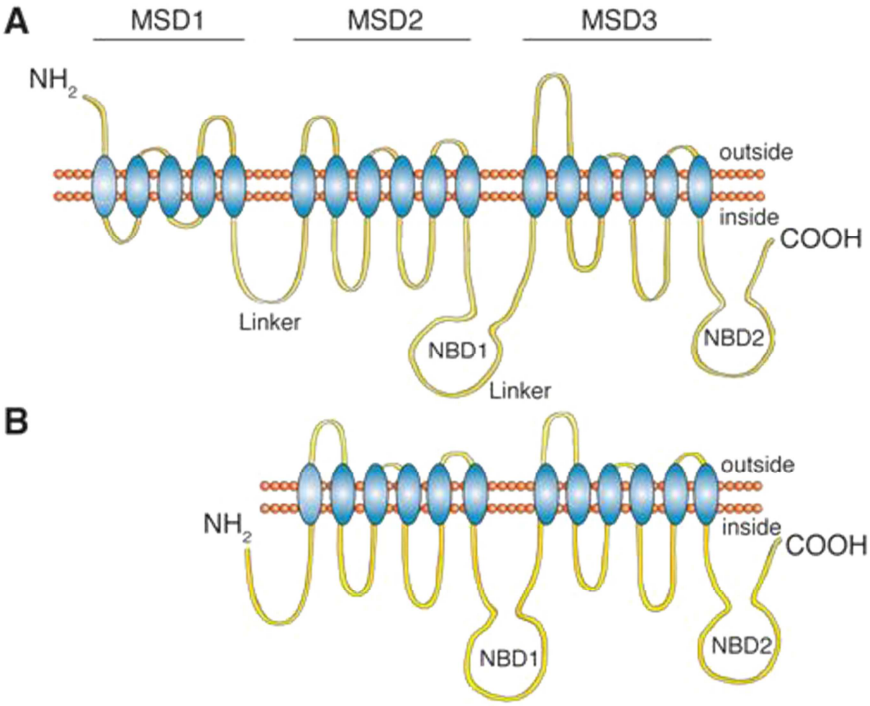
In cancer

In cell lines: In terms of cancer, the ABCC10 gene is expressed in human tumor cell lines, HepG2, CWR22RV1 and TSU-PR1 at greater or equal levels than ABCC1, ABCC2 and ABCC3. Novel ABCC10 transcripts have been identified in HepG2, and CWR22RV1 cells. These transcripts are heterogeneic and imply complexity in the exons and introns of this region (Dabrowska and Sirotnak, 2004).

In breast cancer: ABCC10 transcript is upregulated in breast tumors treated with 5-fluorouracil, anthracycline, cyclophosphamide or taxane based neoadjuvant chemotherapy in comparison with normal tissue. Further, ABCC10 transcript expression is associated with ER positive breast cancer (Hlavac et al., 2013).

In acute myeloid leukemia: ABCC10 transcript is also expressed in acute myeloid leukemia (Hu et al., 2011).

In hepatocellular carcinoma: Transcripts from ABCC10 and various other transporters including: ABCB6, ABCC1, ABCC4, ABCC5, and ABCC12 are upregulated in over 50% hepatocellular carcinoma in untreated patients. It was also observed that microRNA let-7a/e is able to downregulate ABCC10 transcript (Borel et al., 2012).



Protein

Description

Unglycosylated ABCC10 is ~158 kDa (Hopper et al., 2001).

ABCC10, like ABCC1, 2, 3 and 6 (see figure above A) has an N-terminal membrane spanning domain (MSD) that is not present in ABCC4, 5, 11 or 12 (figure above B). All ABCC subfamily members contain two Nucleotide Binding Domains (NBD).

Expression

ABCC10 has been detected in various human occular-absorption barrier tissues including, the iris ciliary body, corneal epithelium, conjuntive epithelium, and retina (Chen et al., 2013).

ABCC10 is expressed in cell lines derived from acute myeloid leukemia (Hu et al., 2011).

Localisation

Localizes basolaterally in ABCC10-transfected LLC-pK1 cells (Malofeeva et al., 2012).

Function

In vitro

ABCC10 transports estrogen β glucuronide, and exhibits modest transport of leukotrienes. Similar to other subfamily members ABCC10 can efflux lipophilic anions (Chen et al., 2003).

ABCC10 is a drug efflux pump that is able to mediate transport of taxanes in vivo. In vitro studies have shown that ABCC10 confers resistance to a variety of hydrophobic drugs, including paclitaxel, docetaxel, vincristine, vinblastine, epothilone B, cytarabine, in a glutathione independent manner (Hopper-Borge et al., 2004; Hopper-Borge et al., 2009).

Prior work has shown that ABCC10 may have a role in natural killer cell mediated lysis. A report demonstrated that a peptide derived from ABCC10 binds to HLA-E and inhibits NK cell-mediated lysis in a CD94 and class I-dependent fashion (Wooden et al., 2005).

ABCC10 ATPase activity is stimulated by estradiol glucuronide, leukotriene, tamoxifen, docetaxel and ARA-C (Malofeeva et al., 2012).

In vivo

Abcc10 protects thymus, spleen and bone marrow when exposed to paclitaxel in vivo.

Abcc10 loss promotes loss of white blood cells, increased weight loss and increased lethality in mice exposed to high doses of paclitaxel (Hopper-Borge et al., 2011).

Homology

ABCC10 exhibits structural and/or functional homology with other ABC transporters: CFTR, ABCC1, ABCC2, ABCC3, ABCC6.

However, ABCC10 shares the lowest amino acid identity (33.8%) to ABCC1 compared to ABCC2, ABCC3, ABCC4, ABCC5 and ABCC6 (Hopper et al., 2001).

ABCC10 is present in many species including: drosophila melanogaster, xenopus, saccharomyces cerevisiae, danio rerio, sus scrofa, mus musculus, latimeria chalumnae, felis catus, bos taurus, tetranychus urticae (Schippert et al., 2008; Dermauw et al., 2013).

ABCC10 is present in all placental mammals, similar to other subfamily members, ABCC1,

ABCC3, ABCC4-7, and ABCC9 (Moitra and Dean, 2011).

Implicated in

Non small cell lung cancer

Note

In vitro cellular resistance in non small cell lung cancer. ABCC10 expression is a predictive biomarker for the resistance to paclitaxel in non-small cell lung cancer (Oguri et al., 2008). ABCC10/MRP7 expression is associated with vinorelbine resistance in non-small cell lung cancer (Bessho et al., 2009).

Another study implicated ABCC10 in gemcitabine resistance mechanisms in non small cell carcinoma cell lines (Ikeda et al., 2011).

ABCC10 is overexpressed in NSCLC. The expression of ABCC10 in adenocarcinoma is higher than in squamous cell carcinoma.

ABCC10 expression in adenocarcinoma correlates with pathological grades and TNM stages (Wang et al., 2009).

Head and neck cancer

Note

Multidrug resistance protein 7 expression is involved in cross-resistance to docetaxel in salivary gland adenocarcinoma cell lines (Naramoto et al., 2007).

Ovarian cancer

Note

A ovarian carcinoma xenograft model demonstrated that intermittant docetaxel dosing of tumors promotes upregulation of MRP7 and other drug resistance genes including btubulin III, Akt2, and thioredoxin.

However, when the dosing was continuous the various resistance genes did not upregulate (De Souza et al., 2011).

Acute myeloid leukemia

Note

ABCC10 may play a role in Ara-C resistance mechanisms in acute myeloid leukemia (Hu et al., 2011). ABCC10 transcript is more highly expressed in childhood AML than in many normal samples (Steinbach et al., 2006).

Breast cancer

Note

In metastatic breast cancer, a difference in progression-free survival (PFS) was found between circulating stem cells (CTCs) positive and CTCs-negative patients. PFS was shorter in patients whose CTCs expressed two or more ABCC subfamilies, including ABCC10 (Gradilone et al., 2011).

ABCC10 expression may confer therapeutic resistance in solid breast tumors (submitted, Domanitskaya et al.).

Colorectal cancer

Note

An inverse correlation between ABCC10 transcript and tumor aggressiveness and tumor grade severity was found in colorectal cancer (Hlavata et al., 2012).

Human immunodeficiency virus

Note

ABCC10 polymorphisms contribute to the development of kidney tubular dysfunction (KTD) in some HIV patients (Giacomet et al., 2013). ABCC10 polymorphisms modulate blood levels of the anti HIV drugs tenofivir, and nevapirine (Pushpakom et al., 2011; Liptrott et al., 2012).

Parkinson's disease

Note

ABCC10 inhibits methylmercury-associated animal toxicity and dopaminergic neurodegeneration in Caenorhabditis elegans (Vanduyn and Nass, 2014).

References

Hopper E, Belinsky MG, Zeng H, Tosolini A, Testa JR, Kruh GD. Analysis of the structure and expression pattern of MRP7 (ABCC10), a new member of the MRP subfamily. Cancer Lett. 2001 Jan 26;162(2):181-91

Chen ZS, Hopper-Borge E, Belinsky MG, Shchaveleva I, Kotova E, Kruh GD. Characterization of the transport properties of human multidrug resistance protein 7 (MRP7, ABCC10). Mol Pharmacol. 2003 Feb;63(2):351-8

Kao HH, Chang MS, Cheng JF, Huang JD. Genomic structure, gene expression, and promoter analysis of human multidrug resistance-associated protein 7. J Biomed Sci. 2003 Jan-Feb;10(1):98-110

Dabrowska M, Sirotnak FM. Regulation of transcription of the human MRP7 gene. Characteristics of the basal promoter and identification of tumor-derived transcripts encoding additional 5' end heterogeneity. Gene. 2004 Oct 27;341:129-39

Hopper-Borge E, Chen ZS, Shchaveleva I, Belinsky MG, Kruh GD. Analysis of the drug resistance profile of multidrug resistance protein 7 (ABCC10): resistance to docetaxel. Cancer Res. 2004 Jul 15;64(14):4927-30

Takayanagi S, Kataoka T, Ohara O, Oishi M, Kuo MT, Ishikawa T. Human ATP-binding cassette transporter ABCC10: expression profile and p53-dependent upregulation. J Exp Ther Oncol. 2004 Oct;4(3):239-46

Maher JM, Slitt AL, Cherrington NJ, Cheng X, Klaassen CD. Tissue distribution and hepatic and renal ontogeny of the multidrug resistance-associated protein (Mrp) family in mice. Drug Metab Dispos. 2005 Jul;33(7):947-55

Wooden SL, Kalb SR, Cotter RJ, Soloski MJ. Cutting edge: HLA-E binds a peptide derived from the ATP-binding cassette transporter multidrug resistance-associated protein 7 and inhibits NK cell-mediated lysis. J Immunol. 2005 Aug 1;175(3):1383-7

Steinbach D, Gillet JP, Sauerbrey A, Gruhn B, Dawczynski K, Bertholet V, de Longueville F, Zintl F, Remacle J, Efferth T. ABCA3 as a possible cause of drug resistance in childhood acute myeloid leukemia. Clin Cancer Res. 2006 Jul 15;12(14 Pt 1):4357-63

Naramoto H, Uematsu T, Uchihashi T, Doto R, Matsuura T, Usui Y, Uematsu S, Li X, Takahashi M, Yamaoka M, Furusawa K. Multidrug resistance-associated protein 7 expression is involved in cross-resistance to docetaxel in salivary gland adenocarcinoma cell lines. Int J Oncol. 2007 Feb;30(2):393-401

Oguri T, Ozasa H, Uemura T, Bessho Y, Miyazaki M, Maeno K, Maeda H, Sato S, Ueda R. MRP7/ABCC10 expression is a predictive biomarker for the resistance to paclitaxel in non-small cell lung cancer. Mol Cancer Ther. 2008 May;7(5):1150-5

Schippert R, Schaeffel F, Feldkaemper MP. Microarray analysis of retinal gene expression in chicks during imposed myopic defocus. Mol Vis. 2008 Aug 31;14:1589-99

Bessho Y, Oguri T, Ozasa H, Uemura T, Sakamoto H, Miyazaki M, Maeno K, Sato S, Ueda R. ABCC10/MRP7 is associated with vinorelbine resistance in non-small cell lung cancer. Oncol Rep. 2009 Jan;21(1):263-8

Hopper-Borge E, Xu X, Shen T, Shi Z, Chen ZS, Kruh GD. Human multidrug resistance protein 7 (ABCC10) is a resistance factor for nucleoside analogues and epothilone B. Cancer Res. 2009 Jan 1;69(1):178-84

Szeri F, Iliás A, Pomozi V, Robinow S, Bakos E, Váradi A. The high turnover Drosophila multidrug resistance-associated protein shares the biochemical features of its human orthologues. Biochim Biophys Acta. 2009 Feb;1788(2):402-9

Wang P, Zhang Z, Gao K, Deng Y, Zhao J, Liu B, Li X. [Expression and Clinical Significance of ABCC10 in the Patients with Non-small Cell Lung Cancer.]. Zhongguo Fei Ai Za Zhi. 2009 Aug 20;12(8):875-8

De Souza R, Zahedi P, Badame RM, Allen C, Piquette-Miller M. Chemotherapy dosing schedule influences drug resistance development in ovarian cancer. Mol Cancer Ther. 2011 Jul;10(7):1289-99

Gradilone A, Naso G, Raimondi C, Cortesi E, Gandini O, Vincenzi B, Saltarelli R, Chiapparino E, Spremberg F, Cristofanilli M, Frati L, Aglianò AM, Gazzaniga P. Circulating tumor cells (CTCs) in metastatic breast cancer (MBC): prognosis, drug resistance and phenotypic characterization. Ann Oncol. 2011 Jan;22(1):86-92

Hopper-Borge EA, Churchill T, Paulose C, Nicolas E, Jacobs JD, Ngo O, Kuang Y, Grinberg A, Westphal H, Chen ZS, Klein-Szanto AJ, Belinsky MG, Kruh GD. Contribution of Abcc10 (Mrp7) to in vivo paclitaxel resistance as assessed in Abcc10(-/-) mice. Cancer Res. 2011 May 15;71(10):3649-57

Hu S, Niu H, Inaba H, Orwick S, Rose C, Panetta JC, Yang S, Pounds S, Fan Y, Calabrese C, Rehg JE, Campana D, Rubnitz JE, Baker SD. Activity of the multikinase inhibitor sorafenib in combination with cytarabine in acute myeloid leukemia. J Natl Cancer Inst. 2011 Jun 8;103(11):893-905

Ikeda R, Vermeulen LC, Lau E, Jiang Z, Sachidanandam K, Yamada K, Kolesar JM. Isolation and characterization of gemcitabine-resistant human non-small cell lung cancer A549 cells. Int J Oncol. 2011 Feb;38(2):513-9

Moitra K, Dean M. Evolution of ABC transporters by gene duplication and their role in human disease. Biol Chem. 2011 Jan;392(1-2):29-37

Pushpakom SP, Liptrott NJ, Rodríguez-Nóvoa S, Labarga P, Soriano V, Albalater M, Hopper-Borge E, Bonora S, Di Perri G, Back DJ, Khoo S, Pirmohamed M, Owen A. Genetic variants of ABCC10, a novel tenofovir transporter, are associated with kidney tubular dysfunction. J Infect Dis. 2011 Jul 1;204(1):145-53

Borel F, Konstantinova P, Jansen PL. Diagnostic and therapeutic potential of miRNA signatures in patients with hepatocellular carcinoma. J Hepatol. 2012 Jun;56(6):1371-83

Hlavata I, Mohelnikova-Duchonova B, Vaclavikova R, Liska V, Pitule P, Novak P, Bruha J, Vycital O, Holubec L, Treska V, Vodicka P, Soucek P. The role of ABC transporters in progression and clinical outcome of colorectal cancer. Mutagenesis. 2012 Mar;27(2):187-96

Liptrott NJ, Pushpakom S, Wyen C, Fätkenheuer G, Hoffmann C, Mauss S, Knechten H, Brockmeyer NH, Hopper-Borge E, Siccardi M, Back DJ, Khoo SH, Pirmohamed M, Owen A. Association of ABCC10 polymorphisms with nevirapine plasma concentrations in the German Competence Network for HIV/AIDS. Pharmacogenet Genomics. 2012 Jan;22(1):10-9

Malofeeva EV, Domanitskaya N, Gudima M, Hopper-Borge EA. Modulation of the ATPase and transport activities of broad-acting multidrug resistance factor ABCC10 (MRP7). Cancer Res. 2012 Dec 15;72(24):6457-67

Chen P, Chen H, Zang X, Chen M, Jiang H, Han S, Wu X. Expression of efflux transporters in human ocular tissues. Drug Metab Dispos. 2013 Nov;41(11):1934-48

Dermauw W, Osborne EJ, Clark RM, Grbić M, Tirry L, Van Leeuwen T. A burst of ABC genes in the genome of the polyphagous spider mite Tetranychus urticae. BMC Genomics. 2013 May 10;14:317

Giacomet V, Cattaneo D, Viganò A, Nannini P, Manfredini V, Ramponi G, Clementi E, Zuccotti GV. Tenofovir-induced renal tubular dysfunction in vertically HIV-infected patients associated with polymorphisms in ABCC2, ABCC4 and ABCC10 genes. Pediatr Infect Dis J. 2013 Oct;32(10):e403-5

Hlaváč V, Brynychová V, Václavíková R, Ehrlichová M, Vrána D, Pecha V, Koževnikovová R, Trnková M, Gatěk J, Kopperová D, Gut I, Souček P. The expression profile of ATP-binding cassette transporter genes in breast carcinoma. Pharmacogenomics. 2013 Apr;14(5):515-29

VanDuyn N, Nass R. The putative multidrug resistance protein MRP-7 inhibits methylmercury-associated animal toxicity and dopaminergic neurodegeneration in Caenorhabditis elegans. J Neurochem. 2014 Mar;128(6):962-74

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